



Study of Insulin Resistance and Metabolic Syndrome in Female Hypothyroid Patients - A Cross Sectional Study

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INTRODUCTION

Hypothyroidism is a common endocrine disorder in the adult population resulting from deficiency of thyroid hormone. Incidence of hypothyroidism increases with age. The prevalence of hypothyroidism is 9.3% in women and 1.3% in men in the world. Hypothyroidism is associated with obesity, dyslipidemia and increased atherosclerotic vascular disease.

Hypothyroidism is a risk factor for insulin resistance, hyperlipidemia, hypercoagulability, low grade inflammation and increased risk for other metabolic disorders such as diabetes and prediabetes called metabolic syndrome.

A possible pathogenic mechanism involved in insulin resistance in hypothyroidism is the decreased blood flow in the peripheral tissues. Hypothyroidism results in decreased hepatic glucose output thereby compensating for insulin resistance present in peripheral tissues and accounting for the diminished insulin requirement

for glycemic control in hypothyroid diabetic patients as regards to beta cell function normal or reduced basal plasma insulin levels have been described in hypothyroidism. These findings are quite consistent with the idea of attenuated endogenous glucose production in the hypothyroid state.

Homeostatic model assessment (HOMA) is a method for assessing beta cell function and insulin resistance from fasting glucose and insulin or C-peptide concentrations. The homeostatic model assessment for insulin resistance derives estimates of insulin sensitivity from the mathematical formula using fasting plasma glucose and insulin concentrations. Insulin resistance leads to an increased production of hepatic cholesterol, very low density lipoproteins and increased high density lipoproteins cholesterol clearance. Insulin resistance augments the deleterious effects of hypothyroidism on lipid profile.

Metabolic syndrome is generally characterized as a clustering of the abnormal levels of blood lipids (low HDL and high triglycerides) impaired fasting glucose, elevated blood pressure and excess abdominal obesity. Obesity, insulin resistance, physical inactivity, advanced age and hormonal imbalance have been suggested as the underlying risk factor for the development of the syndrome. People with metabolic syndrome are at increased risk of atherosclerotic cardiovascular disease and type II diabetes.

The study is to find out the relationship between thyroid function and insulin resistance in female hypothyroid patients and whether hypothyroidism is associated with metabolic syndrome. This study may be used for improving cardiovascular risk assessment.

REVIEW OF LITERATURE

Thyroid disease in the general population is 6.6%. it is much more common in females than males.

Thyroid disease in diabetes:

Overall prevalence: 10.813%

Hypothyroidism	: 36%
Subclinical hypothyroidism	: 5.10%
Hyperthyroidism	: 12%
Postpartum thyroiditis	: 11%
Others	: 35.87%

The reduction in thyroid hormone action is secondary to reduced thyroid hormone synthesis and secretion by the thyroid glands.

SYMPTOMS

- Fatigue and lethargy
- Weight gain
- Decreased appetite
- Cold intolerance
- Dry skin
- Hair loss
- Drowsiness
- Muscle pain, joint pain, weakness in the extremities
- Depression
- Emotional lability, mental impairment
- Impaired memory, inability to concentrate
- Constipation

- Menstrual disturbances, impaired fertility
- Decreased perspiration
- Paresthesia and nerve entrapment syndromes
- Blurred vision
- Fullness in throat, hoarseness

The diagnosis of hypothyroidism is based on finding a low free thyroxine (fT₄) level, usually with an elevation in the thyroid stimulating hormone (TSH) levels.

THYROID FUNCTION TESTS

Normal laboratory values

Test	Abbreviation	Normal ranges
Serum Thyroxine	T ₄	4.6 – 12 µg/dl
Free thyroxine	fT ₄	0.7 – 1.9 ng/dl
Serum triiodothyronine	T ₃	0.52 – 1.85 nmol/dl
Free triiodothyronine	fT ₃	1.4 – 4.2 pmol/dl
Serum thyrotrophin	TSH	0.5 – 6 µIU/ml

AIMS AND OBJECTIVES

PRIMARY OBJECTIVE

1. To investigate the relationship between thyroid function and insulin resistance in female hypothyroid patients.
2. To investigate the relationship between thyroid function and metabolic syndrome in female hypothyroid patients.

SECONDARY OBJECTIVE

1. To assess the serum insulin level & HOMA-IR (homeostasis model assessment – insulin resistance index) in female hypothyroid patients.
2. To study the correlation of lipid profile parameters (TC, TG, HDL, LDL) with thyroid function in female hypothyroid patients.

MATERIALS AND METHODS

STUDY POPULATION

Newly diagnosed and untreated female hypothyroid patients of age between 18 to 45 years and those visiting the special investigation laboratory under Department of Biochemistry, Government /medical College Hospital, Thiruvananthapuram during the period of study (December 2010 to December 2011).

EXCLUSION CRITERIA

- Patients with known thyroid dysfunction or on medications
- Patients with diabetes mellitus
- Patients with polycystic ovarian disease
- Patients with tuberculosis
- Patients with liver disorders
- Patients with renal disorders
- Patients with congestive cardiac failure
- Patients on oral contraceptive pills
- Patients on statins
- Patients on other medications that alter thyroid functions and lipid levels
- Patients with pregnancy
- Postmenopausal patients
- Patients with other systemic illness

STUDY DESIGN

This study was a cross sectional study by design and the period of study was from December 2010 to December 2011. The study group consisted of 100 newly diagnosed and untreated female hypothyroid patients visiting the thyroid laboratory under department of biochemistry.

DATA COLLECTION

The study was conducted only after approval of the ethical committee of Government Medical College Thiruvananthapuram

The anthropometric parameters recorded are weight, height, waist measurement, hip measurement, B.P, body mass index, & waist hip ratio.

The biochemical parameters estimated were serum insulin, fT₃, fT₄, T₃,T₄, TSH, FBS, fasting lipid profile.

RESULTS & DISCUSSION

Hypothyroidism is a common endocrine disorder which is associated with obesity, dislipidemia and increased atherosclerotic vascular disease. It is a risk factor for insulin resistance, hyperlipidemia, hypercoagulability, low grade inflammation and increased risk for other metabolic disorders such as diabetes and prediabetes called metabolic syndrome.

Hypothyroidism is associated with an elevated risk of cardiovascular disease and adverse changes in lipids. At low insulin sensitivity, increases in TSH levels are associated with marked changes in lipid risk factors & thus cardiovascular risk. Measurement of insulin resistance might improve the prediction of cardiovascular disease and diabetes mellitus in patients with hypothyroidism and by reducing insulin resistance we can prevent those complications.

This cross sectional study was done to investigate the relationship between the thyroid function, insulin resistance and metabolic syndrome in female hypothyroid patients. The serum insulin level, HOMA-IR and the correlation of lipid profile parameters in female hypothyroid patients were also studied.

In the present study 100 women with hypothyroidism in age group 18-45 was taken as cases. Correlation of serum insulin and HOMA-IR with thyroid function for the study group showed that TSH was positively correlated and T₃, T₂, fT₃, fT₄ were negatively correlated with serum insulin the results obtained in relation to thyroid function was comparable with sat Byul park et al.

In the present study, out of 100 cases 90 had insulin resistance and 88 had metabolic syndrome. In the present study 90% of the cases have insulin resistance, among these 90 cases, 85 cases[94.4%] were affected with metabolic syndrome whereas only 30% of the noninsulin resistance group were affected by metabolic syndrome. The observed difference was statistically significant [p<.05]. The results obtained in relation to thyroid function was comparable with Demidova et al.

Comparison of Insulin Resistance and Metabolic Syndrome in the Study Group

Insulin resistance	Metabolic syndrome				Total	
	Absent		Present			
	N	%	N	%	N	%
Absent	7	70.0	3	30.0	10	10.0
Present	5	5.6	85	94.4	90	90.0
Total	12	12.0	88	88.0	100	100.0

Fisher's Exact test p<.001

Luboshitzky et al had observed that the percentage of metabolic syndrome in hypothyroid patient was significantly higher than in controls.

Hypothyroidism had significantly higher likelihood of cardiovascular risks. Hypothyroid patients had significantly higher triglyceride levels and glucose levels compared with controls. Although body mass index values were similar in both groups, patients had greater waist circumference than controls. The percentages of hypothyroid patients had greater waist circumference than controls. The percentages of hypothyroid patients having hypertension, hypertriglyceridaemia, hyperglycemia, and greater waist circumference were higher than the percentages in controls. In a study by R V Jayakumar et al, it was reported that 60 percent of the cases with metabolic syndrome had thyroid function abnormalities in their case series.

In the present study patients with hypothyroidism had significantly higher HOMA-IR and the mean insulin level increases with increase in TSH level in cases with hypothyroidism leading to hyperinsulinaemia. Similarly Tuzcu et al observed that hypothyroidism was associated with fasting hyperinsulinaemia.

Levels of TSH In Patients With Hypothyroidism Comparison of Serum Level with Different

TSH	No of patients	Insulin	
		Mean	Sd
<20	24	13.3	3.1
20-40	47	16.6	4.4
40-60	20	22.5	7.6
60-80	6	28.2	9.6
>80	3	32.7	5.7
Total	100	18.2	7.1

Anova test was done. p value < 0.001.

Comparison of HOMA group with TSH group

		TSH group		Total	
		Group I	Group II		
HOMAgrou p	<3	Count	10	0	10
		% within TSH group	14.1%	0%	10.0%
	≥3	Count	61	29	90
		% within TSH group	85.9%	100.0%	90.0%
Total		Count	71	29	100
		% within TSH group	100.0%	100.0%	100.0%

In the present study, TSH was positively correlated and fT_3 , fT_4 , T_3 , T_4 was negatively correlated with total cholesterol and LDL which was statistically significant. TG was positively correlated with TSH and HDL was negatively correlated with TSH which was statistically insignificant.

In the present study, the study population was divided into two groups according to the TSH levels as group I [TSH level 6-40] and group [TSH above 40]. mean values of T_3 , T_4 , TC, TG, HDL, LDL, Insulin HOMA and BMI compared between these two groups and the observed difference of mean values of T_3 , T_4 , TC, LDL, Insulin and HOMA IR were statistically significant [p<05] The difference in TG and HDL were not statistically significant

In a study Regmi et al, the TC and LDL were increased progressively with the increasing TSH values.¹⁴¹ This was comparable to the findings in my study

This cross sectional study showed that serum insulin level and HOMA –IR were increased in female hypothyroid patients and the frequency of metabolic syndrome was also increased in our study. This was in accordance with several epidemiological studies which had shown that insulin resistance and metabolic syndrome were seen and hypothyroidism

LIMITATION

- Our study was cross – sectional, so its ability to infer causality is limited.
- We were unable to comment on the effect of hormone replacement for insulin

- Resistance in patients hypothyroidism due to lack of follow up data.
- Our sample size was also small so further cohort studies with larger sample size is needed to establish the association of insulin resistance with different parameters.
- Population based studies are required to validate our study findings in a broader perspective

CONCLUSION

- ❖ There was significant correlation of serum insulin & HOMA-IR with thyroid function.
- ❖ Higher levels of TSH may predict the insulin resistance and metabolic syndrome.
- ❖ Insulin resistance and metabolic syndrome were increased in patients with hypothyroidism.
- ❖ There was significant increase in serum insulin level as TSH level increases.
- ❖ In hypothyroid patients with insulin resistance, the frequency of metabolic syndrome was significantly higher than in hypothyroid non insulin resistance group.
- ❖ As the frequency of insulin resistance was increased in hypothyroid patients, they were at increased risk for metabolic disorders, such as pre-diabetes or diabetes mellitus.
- ❖ Hypothyroid patients had significantly high total cholesterol and LDL as TSH increases and there was significant correlation of total cholesterol and LDL with thyroid function.
- ❖ Insulin resistant and dyslipidaemic patients are at higher risk of cardiovascular disease.

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